



UNITED STATES PATENT AND TRADEMARK OFFICE

W
UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,005	10/02/2003	Norman L. Anderson		6420
7590	03/10/2006		EXAMINER	
Hendricks and Associates P. O. Box 2509 Fairfax, VA 22031-2509			HINES, JANA A	
			ART UNIT	PAPER NUMBER
			1645	

DATE MAILED: 03/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/676,005	ANDERSON, NORMAN L.
	Examiner	Art Unit
	Ja-Na Hines	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 23 December 2005.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-43 is/are pending in the application.
4a) Of the above claim(s) 3,6,27-36,42 and 43 is/are withdrawn from consideration.
5) Claim(s) _____ is/are allowed.
6) Claim(s) 1-26 and 37-41 is/are rejected.
7) Claim(s) _____ is/are objected to.
8) Claim(s) 1-43 are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 2/17/06.

4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ .
5) Notice of Informal Patent Application (PTO-152)
6) Other: ____ .

DETAILED ACTION

Amendment Entry

1. The amendment filed December 23, 2005 has been entered. Claims 1, 14 and 23 have been amended.

Election/Restrictions

2. Applicant's election of Group I in the reply filed on December 23, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 27-36 and 42-43 have been withdrawn from consideration. Claims 1-26 and 37-41 are under consideration in this office action.

Priority

3. If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 120, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

Specification

4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

5. Claims 2 and 38 are objected to because of the following informalities: Claim 2 lacks a period at the end of the sentence. Claim 38 recites "the label the label". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-26 and 37-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a method for quantifying the amount of at least one target protein in a sample comprising: a digestion step; preparing at least one labeled monitor peptide comprising a subsequence of said target protein(s) to provide an internal standard; an addition step; a loading step; a washing step; an elution step and a subjecting step. The written description in this case does not set forth what the subsequence of the target protein is, therefore the written description is not commensurate in scope with the claims drawn to the subsequence.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude, "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the

conclusion that the applicant was in possession of the claimed species is sufficient.” MPEP 2163.

Furthermore, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.*, the court stated:

“A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. *Fiers*, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) (“In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . .”). *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is “not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.” MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In *Gostelli*, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872 F.2d at 1012, 10 USPQ2d at 1618.

In this case, neither the specification nor the claims teach how to define the subsequence. Neither do the claims nor the specification teach which regions of the target protein can or cannot comprise the subsequence. The specification does not include structural examples of those subsequences. Thus, the subsequence could result in a complex not taught and enabled by the specification. The generic statements drawn to the subsequence do not provide ample written description for the subsequence since neither the specification nor the claims describe a single structural feature associated with the subsequence. The specification fails to provide examples of what the actual identity of the subsequence is. As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 1 is a broad generic claim with respect all possible subsequences encompassed by the claim. The possible structural variations are limitless. It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the subsequence. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives.

Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession

of the entire scope of the claimed invention. In view of these considerations, a person skilled in the art would not have viewed the teachings of the specification sufficient to show that applicants were in possession of a method for quantifying the amount of at least one target protein in a sample comprising: preparing at least one labeled monitor peptide comprising a subsequence of said target protein(s) to provide an internal standard. Therefore the full breadth of the claim fails to meet the written description provision of 35 USC 112, first paragraph.

7. Claims 1-26 and 37-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- a) Claim 1 recites the limitation "the product" in the claim several times. There is insufficient antecedent basis for this limitation in the claim.
- b) Claim 1 (3) refers to the product of step 2 containing labeled synthetic peptide, however it is unclear where this synthetic peptide came from. It is unclear the synthetic peptide became contained in the aliquot of at least one labeled monitor peptide comprising a subsequence of said target protein. Therefore clarification is required to overcome the rejection.
- c) Claim 1(7) recites the limitation "the labeled synthetic standard." in the claim. There is insufficient antecedent basis for this limitation in the claim.

d) Claim 1(7) refers the labeled synthetic standard. It is unclear if applicant intends to be referring to the labeled synthetic peptide or the internal standard. Therefore clarification is required to overcome the rejection.

e) Claim 1(7) is unclear. It is unclear how the monitor peptide is compared to the labeled synthetic peptide because step 5 removed unbound peptide, including the synthetic peptide. Therefore it is unclear how the removed synthetic peptide is now available for comparison. Thus, clarification is required to overcome the rejection.

f) Claim 2 is unclear. The claim refers to a mixture thereof, however it is unclear what components are in the mixture thereof.

g) Claim 2 recites the limitation "the label" in the claim. There is insufficient antecedent basis for this limitation in the claim.

h) Claim 2 recites that there is a label; however claim 1 does not refer to just a label. Rather claim 1 refers to labeled monitor peptides or labeled synthetic peptides. Therefore it is unclear if the label is referring to labeled monitor peptides and/or labeled synthetic peptides or something else. Thus clarification is required to overcome the rejection.

i) Claims 11-13 recite the limitation "the solid support" in the claims. There is insufficient antecedent basis for this limitation in the claim.

j) Claim 15 is unclear. The claim refers to the support to which the binding agent bind has a hydrophilic plastic. It is unclear if the hydrophilic plastic refers to the support or the binding agent. Therefore, clarification is required to overcome the rejection.

k) Claims 19-20 recite the limitation "the flow path" in the claims. There is insufficient antecedent basis for this limitation in the claim.

l) Claims 21-22 refer to "the peptides" however it is unclear which peptides are being referred to, i.e., the peptides of step 1, the labeled monitor peptide, the labeled synthetic peptide or some other peptide. Therefore clarification is required to overcome the rejection.

m) Claims 21-22, 25-26 and 36 recite the limitation "the mass spectrometer" in the claims. There is insufficient antecedent basis for this limitation in the claim.

n) Claim 21 refers to the peptides being fragmented after introduction into the mass spectrometer, however it is unclear whether the claim is stating that the peptides were not fragmented or digested as in step 1 or if the peptides are fragmented a second time. Therefore clarification is required to overcome the rejection.

o) Claim 23 is unclear because of the phrase "differ but in mass..". It is unclear how the labeled monitor peptides differ since the term is relative. The metes and bounds of the term have not been disclosed by the specification therefore the claim is unclear. It is also unclear as to what the claim is requiring. It is unclear as to how to interpret that when different labeling atoms are used to label a specific synthetic peptide so that the label monitor peptides having the same amino acid sequence differ but in mass from the target protein. Therefore clarification is required to overcome the rejection.

p) Claims 24 and 26 recite the limitation "the mixture" in the claim. There is insufficient antecedent basis for this limitation in the claim.

q) Claims 38 recite the limitation "the label" in the claim. There is insufficient antecedent basis for this limitation in the claim.

r) Claim 38 recites that there is an introduction of the label; however claim 1 never introduces just a label. Rather claim 1 refers to labeled monitor peptides or labeled synthetic peptides. Therefore it is unclear how the label is or is not introduced. Thus clarification is required to overcome the rejection.

s) Claim 41 is unclear for the same reason as claim 38. Therefore clarification is required to overcome the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1-5, 11-15, 19-20 and 37-41 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Geng et al.

The claims are drawn to a method for quantifying the amount of at least one target protein in a sample comprising the steps of:

1. digesting the sample to provide peptides; 2. preparing at least one labeled monitor peptide comprising a subsequence of said target protein(s) to provide an internal standard; 3. adding an aliquot of the product of step 2 containing a known amount of labeled synthetic peptide to the product of step 1; 4. loading the product of step 3 onto at least one support which has attached thereto at least one binding agent which binds to at least one monitor peptide; 5. washing the support(s) of step 4 to remove unbound peptides; 6. eluting the monitor peptide(s) from the binding agent(s) bound to the support(s); 7. subjecting at least one of the monitor peptides present in the eluate(s) obtained in step 6 to mass spectrometry to determine the amount of monitor peptide(s) in the digest by comparison with the labeled synthetic standard(s). The dependant claims are drawn to the types of labels, the types of supports, differently labeled peptides, and chemical modification caused by the labels.

Geng et al., teach signature peptide approaches to detecting proteins in complex mixtures. Proteins in complex mixtures were digested to create classes of peptide fragments (abstract). The sample was digested and then stopped (page 298), just as required by the claims. Classes of peptide fragments were selected by affinity chromatography, lectin columns (abstract). The digested samples were injected onto the column (page 298). Thus the column or support is a packed column, having at least one opening and is made of hydrophilic plastic, just as required by the claims. The analytes displaced from the column were then eluted (page 298). Geng et al., teach

silica based columns, thereby teaching monolithic porous beads as the support (pages 298 and 300). Geng et al., teach sequential loading and elution of the products (page 298). Also taught is a wash of the column which removed unbound analyte (page 298). Several purification techniques were disclosed, including serial lectin affinity columns, anion-exchange chromatography or capillary electrophoresis as being used to separate the fractionated peptides (page 299). These purification techniques would have a flow path, thereby teaching the limitations drawn to the flow path. The eluted peptides were monitored and fractions were collected for MALDI-time of flight mass spectrometry analysis (MALDI-TOF-MS) (page 298).

Affinity selected peptide mixtures were transferred to a high resolution reversed-phase chromatography column and further resolved into fractions that were collected and subjected to MALDI-MS (abstract). Geng et al., teach the synthesis of *N*-acetoxy succinamide, *N*-acetoxy succinamide and $d_3\text{-C}^1\text{N}$ -acetoxy succinamide as different isotopic labels added to the peptides (page 298). Thus the art teaches that labels were introduced by chemical modification resulting in the attachment of additional amino acids just as required by the claims. Furthermore the art teaches at least two differently labeled peptides being prepared and loaded onto the support system and mass spectrometer, just as required by the claims. Isotopic labeling can be done through the synthesis of peptides in which one amino acid is labeled or by derivatizing peptides with an isotopically labeled reagent (page 308). Thus the label was introduced by chemical modification, just as required by the claims. The MALDI-TOF-MS was performed using a mass spectrometer (page 298), just as required by the claims. The

data teaches that proteins may be quantified as signature peptides using isotopically labeled internal standards (abstract). The equations were deduced from the ratios of deuterium-labeled and unlabeled acetylated peptides (page 299). Isotopes ratios of peptides were determined by MALDI-MS and used to determine the concentration of a peptide relative to that of the labeled internal standard peptides (abstract).

Thus Geng et al., teach all the steps of the instantly claimed method of quantification including the different supports, the use of differently labeled peptides, and the chemical modification associated with the use of those labels, however Geng et al., do not teach the use of other well known isotope labels such as ¹³C or ¹⁸O.

However, it would have been *prima facie* obvious at the time of applicants' invention to modify the method for quantifying the amount of at least one target protein in a sample as taught by Geng et al., to include the use of other well known isotope labels. One would have a reasonable expectation of success in incorporating other isotopes since no more than routine skill would have been required to exchange the nitrogen or carbon labels taught for the prior art for ¹³C or ¹⁸O. Thus one having ordinary skill in the art would have been motivated to make such a change since only the expected results would have been obtained. Furthermore the use of a known member of a class of isotope label materials is not patentable if other members of the class of isotope label materials were known to be useful for that same purpose. Moreover, the prior art clearly teaches the same digestion step, preparation step, addition step, loading step, washing step, elution step and subjection step just as instantly claimed.

9. Claims 6-8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geng et al., and Niederkofler et al.

The claims are drawn to a method for quantifying the amount of at least one target protein in a sample comprising a: digestion step, preparation step, addition step, loading step, wash step, elution step and subjection step. The dependant claims are drawn to the types of binding agents used. Geng et al., have been discussed above, however Geng et al., do not teach the use of antibodies as binding agents.

Niederkofler et al., teach an antibody-derivatized affinity pipet tip system used for the parallel extraction of specific proteins from a sample and subsequent deposition onto 96-well arrayed matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF-MS) targets (page 3294). The use of anti-B₂ microglobulin IgG antibodies on affinity tips allowed for purification (page 3295). Affinity purified polyclonal B₂m antibody was also used in the experimental procedure (page 3295). Thus the art teaches the use of monoclonal and polyclonal antibodies as binding agents, just as required by the claims. Furthermore, it is well known in the art that antibodies are recyclable and do not lose their ability to bind after just one binding event. After incubation the retained species were eluted from the affinity pipet tips using MALDI matrix and were introduced into the mass spectrometer (page 3295). Then the mass spectrometry was performed using a MALDI-TOF mass spectrometer (page 3296).

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the method for quantifying the amount of at least one target protein

in a sample as taught by Geng et al., wherein the modification uses antibody binding agents as taught by Niederkofler et al. One would have a reasonable expectation of success in incorporating other binding agents into the method since no more than routine skill would have been required to exchange the binding agents of Geng et al., for those of Niederkofler et al., since Geng et al., teach that affinity purification is useful in such methods. Furthermore, only routine skill is required since both Geng et al., and Niederkofler et al., both teach methods for quantifying the amount of at least one target protein in a sample by means of a purification step, a wash step, an elution step and subjection step, just as instantly claimed. Thus one having ordinary skill in the art would have been motivated to make such a change since only the expected results would have been obtained. Furthermore the use of a known member of a class of binding agent materials is not patentable if other members of the class of binding agent materials were known to be useful for that same purpose.

10. Claims 16-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geng et al., and Wall et al.

The claims are drawn to a method for quantifying the amount of at least one target protein in a sample comprising a: digestion step, preparation step, addition step, loading step, wash step, elution step and subjection step. The dependant claims are drawn to the types of supports used. Geng et al., have been discussed above, however Geng et al., do not teach the use of the different types of instantly claimed supports.

Wall et al., teach two-dimensional liquid phase separation method which is capable of resolving large numbers of cellular proteins for mapping of cellular proteins with identification using matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF-MS). Protein purification procedures such as 2-D PAGE uses gel as the separation medium (page 1100). Also taught was a 1-D gel and SDS PAGE separation of the proteins (page 1101). Other purification techniques include isoelectric focusing, and nonporous reversed phase HPLC (page 1100). These techniques teach a variety of supports wherein hydrophobic plastic used in isoelectric focusing, or in the alternative using mesh or gel supports, just as required by the claims. Wall et al., teach the variety of separation techniques followed by the MALDI-TOF-MS analysis of isolated proteins (page 1101). Wall et al., do not disclose an initial digestion step. Therefore, Wall et al., teach that the peptides were not fragments, but were detected in the form in which they were introduced into the mass spectrometer, just as required by the claims.

Therefore, it would have been *prima facie* obvious at the time of applicants invention to modify the method for quantifying the amount of at least one target protein in a sample as taught by Geng et al., wherein the modification uses different solid supports as taught by Wall et al. One would have a reasonable expectation of success in incorporating other supports into the method since no more than routine skill would have been required to exchange the supports of Geng et al., for those of Wall et al., since Geng et al., teach that several different purification techniques are useful in methods for quantifying the amount of at least one target protein in a sample.

Furthermore, only routine skill is required since both Geng et al., and Wall et al., both teach methods for quantifying the amount of at least one target protein in a sample by means of a purification step, a wash step, and subjection step, just as instantly claimed. Thus one having ordinary skill in the art would have been motivated to make such a change since only the expected results would have been obtained. Furthermore the use of a known member of a class of solid support materials is not patentable if other members of the class of solid support materials were known to be useful for that same purpose.

Prior Art

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Zhang et al., teach fractionation of isotopically labeled peptides in quantitative proteomics wherein labeling is achieved by derivatizing peptides with isotopically different forms of a derivatizing agent and quantification is accomplished by mass spectrometry.

Conclusion

12. No claims allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines *JH*
March 2, 2006

LP
LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600